SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Permanent Pacemaker Electrode
Device Trade Name:	Medtronic® SelectSecure™ Lead Model 3830
Applicant's Name and Address:	Medtronic, Inc. 7000 Central Avenue N.E. Minneapolis, MN 55432-3576
Date of Panel Recommendation:	None
Pre-Market Application (PMA) Number:	P030036
Date of Notice of Approval to Applicant:	August 3, 2005

II. INDICATIONS FOR USE

The Medtronic® SelectSecure™ Lead Model 3830 (hereinafter called the Model 3830) has application where implantable atrial or ventricular, single-chamber or dual-chamber pacing systems are indicated. The Model 3830 lead is intended for pacing and sensing in the atrium or ventricle.

III. CONTRAINDICATIONS

The following are contraindications for use of Medtronic implantable, screw-in, transvenous leads.

- Use of ventricular transvenous leads is contraindicated in patients with tricuspid valvular disease.
- Use of ventricular transvenous leads is contraindicated in patients with mechanical tricuspid heart valves.
- Use of steroid eluting transvenous leads is contraindicated in patients for whom a single dose of 40 µg of beclomethasone dipropionate may be contraindicated.
- Use of catheter-delivered transvenous leads is contraindicated in patients with obstructed or inadequate vasculature for intravenous catheterization.

IV. WARNINGS

The Warnings and Precautions can be found in the Model 3830 labeling.

V. PRODUCT DESCRIPTION

The Model 3830 is a device / drug combination product made up of two regulated components: a device (the Medtronic SelectSecure™ lead) and a drug component (beclomethasone dipropionate). The characteristics of the Model 3830 appear in **Table 1**.

Table 1. Design of Model 3830 Lead

Characteristic			Model 3830
Lead Body Diameter			1.37 mm (.054")
Lead Body Length			20 – 110 cm
Introduction Size			9.0 French with catheter / introducer
Tip to Ring Spacing			9 mm
Connector			IS-1 Bipolar
Electrodes	**Tip**	**Material**	Titanium Nitride coated Platinum
		Geometry	Helix
		Surface Area	3.55 mm^2
		Steroid	17.9 µg target dose beclomethasone dipropionate anhydrous
	Ring	**Material**	Titanium Nitride coated Platinum Alloy
		Geometry	Cylindrical
		Surface Area	16.85 mm^2

A. Device Component Description

The Model 3830 lead is a co-axial, bipolar, catheter-delivered, steroid eluting, implantable, transvenous fixed screw pacing lead designed for right atrial and right ventricular pacing and sensing. The lead and accessories are supplied sterile. Each package contains one lead with an anchoring sleeve and one vein lifter.

B. Drug Component Description

The active drug component in the Model 3830 is beclomethasone 17,21-dipropionate (BDP). The chemical name of beclomethasone dipropionate is 9-chloro-11®,17,21-trihydroxy-16®-methylpregna-1,4-diene-3, 20 dione 17,21-dipropionate. The structural formula for beclomethasone 17,21-dipropionate is shown in **Figure 1**.

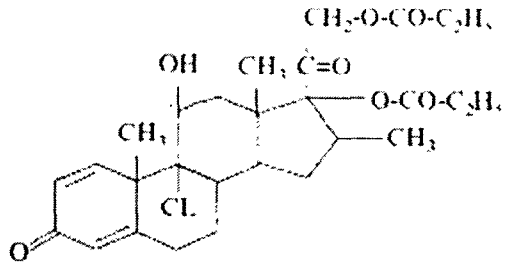

Figure 1: Structural Formula of Beclomethasone 17,21-dipropionate

Beclomethasone 17, 21-dipropionate is a diester of beclomethasone, a synthetic halogenated corticosteroid. Beclomethasone 17, 21-dipropionate is a white to creamy white, odorless powder with a molecular formula of $C_{28}H_{37}ClO_7$ and a molecular weight of 521.05. It is very slightly soluble in water, very soluble in chloroform, and freely soluble in acetone and alcohol.

The target dose of beclomethasone 17, 21-dipropionate on each Model 3830 lead is 17.9 µg.

C. BDP Mechanism of Action

Steroids suppress the inflammatory response that is believed to cause threshold rises typically associated with implanted pacing electrodes. Beclomethasone dipropionate is a synthetic steroid of the glucocorticoid family. Glucocorticoid steroids have potent anti-inflammatory actions via direct and indirect effects on major inflammatory cells. While the mechanism of action of glucocorticoids is not fully understood, it is known that glucocorticosteroids bind to a cytoplasmic glucocorticoid receptor as well as to a membrane-bound receptor. Binding to the cytoplasmic receptor leads to receptor activation and translocation to the nucleus. The receptor interacts with specific DNA sequences (glucocorticoid responsive elements) within the regulatory regions of affected genes. Thus, glucocorticoids inhibit the production by multiple cells of factors that are critical in generating the inflammatory response, in particular via modulation of transcription factors.

VI. ALTERNATIVE PRACTICES OR PROCEDURES

The present established therapies include the use of commercially available pacing leads.

VII. MARKETING HISTORY

The Model 3830 is currently distributed commercially outside the United States. Specifically, this lead is approved for sale in the European Union, Canada, and Australia.

The lead has not been withdrawn from the market in any country for any reason related to the safety or effectiveness of the device.

VIII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

A. Potential Adverse Events

The potential complications (listed in alphabetical order) related to the use of transvenous leads include, but are not limited to, the following patient-related conditions that can occur when the lead is being inserted and/or repositioned:

- Cardiac perforation
- Cardiac tamponade
- Fibrillation and other arrhythmias
- Heart wall or vein wall rupture
- Infection
- Muscle or nerve stimulation
- Pericardial rub
- Pneumothorax
- Air embolism
- Thrombosis/thromboemboli
- Valve damage (particularly in fragile hearts)
- Loss of capture (intermittent or continuous) or continuous loss of sensing due to:
  - Lead dislodgement
  - Lead conductor or helix fracture or insulation failure
  - Threshold elevation or exit block

B. Observed Adverse Events

A clinical study of the Model 3830 began on August 9, 2002. As of July 16, 2004, there were 264 patients implanted with the Model 3830 in the United States, Canada, and Australia. Data from 264 patients enrolled and implanted include 86 roll-in and 178 non-roll-in patients. 176 patients were implanted with a 3830 lead in the atrium while 177 patients were implanted with a 3830 lead in the ventricle. Each implanting investigator was required to first implant two patients that are followed per the protocol but not included in the analysis of any of the objectives other than secondary objective #3 (refer to summary of

clinical studies). These roll in patients give each implanter experience with the new lead so that subsequent implants will more appropriately represent the true performance of the lead. One non-roll-in patient was determined not to meet inclusion criteria due to a prior history of valvular disease and is not included in the analyses for any objectives.

Investigators were asked to report the incidence of adverse events that patients experienced during the clinical study according to the definitions in the protocol. Each adverse event was to be recorded on an adverse event case report form. The case report form includes a description of the event, the relatedness of the event, action taken and the event outcome.

The adverse event was considered lead related if it was a direct result of or was affected by the presence or performance of the investigational lead. All cardiovascular events were further classified as either a complication or an observation based on the following definitions:

- Complication – An adverse event which is resolved invasively or which directly results in the death of or serious injury to the patient, the explant of the device, or the termination of significant device function regardless of other treatments. Intravenous and intramuscular drug therapies are considered invasive treatment.

- Observation – An adverse event, which is resolved by non-invasive means such as medically or by reprogramming the device or which resolves spontaneously. Oral drugs are considered non-invasive treatment.

All lead related events on non-roll-in patients reported by July 16, 2004, appear in **Table 2** (atrial) and **Table 3** (ventricular).

In the 178 non-roll-in patients, there were 15 atrial lead related adverse events occurring in 14 patients. Of these 15 events, 5 were complications (in 5 patients). There were 30 ventricular lead related adverse events occurring in 28 patients. Of these 30 events, 12 were complications (in 12 patients).

As of July 16, 2004, a total of 14 deaths were reported in the study (4 deaths occurred in roll-in patients and 10 deaths occurred in non-roll-in patients). No leads were explanted and returned to Medtronic for analysis. The Adverse Event Advisory Committee (AEAC) classified the deaths as follows: four deaths as non cardiac, seven deaths as non-sudden cardiac, one death as sudden cardiac, and two deaths as unknown. One death was classified as device related due to cardiac perforation.

Table 2: Atrial Lead Related Adverse Events – of the 177 non roll-in patients

Adverse Event	Complications		Observations		Total Events	
	Number of Events	Number of Patients	Number of Events	Number of Patients*	Number of Events	Number of Patients*
Elevated pacing thresholds	0	0	4	4	4	4
Failure to sense / undersensing	2	2	1	1	3	3
Lead dislodgment	2	2	1	1	3	3
Muscle Stimulation	0	0	2	1	2	1
Afib/Aflutter	0	0	1	1	1	1
Pocket Infection	1	1	0	0	1	1
Venous Occlusion	0	0	1	1	1	1
Total	5	5	10	9	15	14
*Not mutually exclusive						

Table 3: Ventricular Lead Related Adverse Events – of the 177 non roll-in patients

Adverse Event	Complications		Observations		Total Events	
	Number of Events	Number of Patients	Number of Events	Number of Patients*	Number of Events	Number of Patients*
Elevated pacing thresholds	2	2	12	12	14	14
Pericardial effusion	3	3	1	1	4	4
Lead dislodgment	3	3	0	0	3	3
Failure to capture/ loss of capture	1	1	1	1	2	2
Muscle stimulation	0	0	2	2	2	2
Cardiac perforation	0	0	1	1	1	1
Chest pain / angina pectoris	1	1	0	0	1	1
Pocket infection	1	1	0	0	1	1
Tamponade	1	1	0	0	1	1
Venous Occlusion	0	0	1	1	1	1
Total	12	12	18	17	30	28
* not mutually exclusive						

IX. Summary of Pre-Clinical Studies

A series of non-clinical laboratory studies was performed on the drug substance and the lead.

A. Biocompatibility Studies

The materials used in the Model 3830 lead that are directly exposed to body tissues or fluids are summarized in **Table 4**. Most of the materials are identical to materials used on previous Medtronic lead designs. Biocompatibility assessment was previously performed in accordance with ISO 10993-1, Biological Evaluation of Medical Devices: Evaluation and Testing. All materials were found to be biocompatible.

Biocompatibility for beclomethasone dipropionate was assessed through electrical and histological evaluation in a canine study (described in part 9D, below).

Table 4: Biocompatibility Information

Material	Where Used in 3830 Lead	Material Used in Current or Previously-Marketed Medtronic Lead Models	FDA Document Control No.
Platinum / Iridium	Ring Electrode and Helix	4092/4592 5024/5524 4024/4524 4074/4574 5076	P830061/S28 P850089/S9 P830061/S12 P830061/34 P930039/S9
Silicone	Inner Insulation Tubing	5076 4092/4592 5054, 5554, 5092, 5592	P930039 /S9 P830061/S28 P850089/S38
Polyurethane 55D	Outer Insulation Tubing	4092/4592 4024/4524	P830061/S28 P830061/S12
MDX Silicone with Barium Sulfate	Anchoring Sleeve	6942	P920015/S12
MDX Silicone	Connector Strain Relief	4023/4024	P830061/S10
Silicone (LSR)	Connector Sleeve	5054, 5554, 5092, 5592	P850089/S38
Steroid Beclomethasone dipropionate	Helix	Drug Master File Master File Authorization Letter	N/A
Titanium Nitride	Electrode coating	4074/4574 Master File Authorization Letter	P830061/S34

B. *In Vivo* Pharmacokinetics

B1. Model 3830 Lead

Pharmacokinetics – The pharmacokinetics (local drug levels and systemic levels) of beclomethasone dipropionate and its metabolites following placement of the SelectSecure Model 3830 leads were not evaluated in the human clinical trial. A preclinical animal study using multiple leads and an assay with a limit of quantitation of 80 pcg/ml did not show any detectable levels of BDP. However, this study did not determine the levels of the active metabolite, beclomethasone-17-monopropionate.

B2. Drug Interactions

No drug interactions with inhaled beclomethasone 17,21-dipropionate have been described. Drug interactions of beclomethasone 17,21-dipropionate with the Model 3830 lead have not been studied.

C. Lead Engineering Testing

Environmental Conditioning: Model 3830 leads were subjected to four cycles of ethylene (EtO) sterilization and five cycles of thermal shock (-45°C to +70°C) prior to undergoing mechanical, electrical, and drug content testing. No damage or degradation to the test leads was noted following sterilization and thermal shock. Leads were then tested according to the summary, below (**Table 5a**). Tests were also conducted on the drug component part of the lead (**Table 5b**).

Table 5a: Bench Testing Summary for Medtronic SelectSecure™ Lead Model 3830

Test	Requirement	Results	Samples Tested
EtO Sterilization	No signs of damage or degradation upon visual examination (minimum magnification 3X) All samples must pass all subsequent mechanical and electrical tests	Passed	28 full leads 22 lead body subassemblies 22 connector subassemblies
Thermal Shock (-45°C-70°C)	No signs of damage or degradation upon visual examination. All samples must pass all subsequent mechanical and electrical tests	Passed	28 full leads 22 lead body subassemblies 22 connector subassemblies
Connector Mating Insertion/ Withdrawal	IS-1 Connector Insertion-Withdrawal forces to be less than 3.15lb-f per ISO 5841-3	Passed	28 full leads
Ventricular Tip Pressure/ Stiffness Testing	Pressure generated at tip of lead when advanced to be less than physiological relevant level.	Passed	28 full leads
Leak Test	No fluid should be observed on the coil or cable upon visual examination	Passed	28 full leads

Table 5a: Bench Testing Summary for Medtronic SelectSecure™ Lead Model 3830			
Test	**Requirement**	**Results**	**Samples Tested**
Lead Composite Torque Test	All lead samples must withstand typical torque loads expected during implant procedure and use without sustaining any visible damage to any joint or component (when viewed with the unaided eye)	Passed	28 full leads
Lead Composite Pull Test	The lead must withstand typical tensile load expected during implant procedure and use without sustaining damage.	Passed	28 full leads
Anchoring Sleeve Suture Test	$\geq$ 0.25 lb minimum breakaway force and no damage to the coil or insulation noted upon visual examination (unaided eye)	Passed	28 lead body assemblies
Lead Body Flex Test	B50 flex life $\geq 2.0 \times 10^5$ cycles at a bend radius of 0.236"	Passed	22 lead body subassemblies
Lead Body Composite Distal Fatigue	No failures of metallic joints or components after 4.0×10^8 cycles.	Passed	18 Samples
Connector Flex	> 82,000 cycles flexed at ±45° without conductor fracture or intermittency	Passed	22 subassemblies
Lead / Catheter Compatibility	Delivery system shall allow necessary positioning of the lead while resulting in no damage to the lead	Passed	23 full leads
DC Resistance	Unipolar 30 ± 7 ohms Bipolar 110 ± 25	Passed	28 full leads
Impedance Between Conductors	Impedance ≥ 50K ohms	Passed	28 full leads
IS-1 Connector Impedance	Impedance ≥ 50K ohms	Passed	28 full leads

Table 5b: Chemistry Manufacturing and Controls Testing for Medtronic Model 3830 Lead			
Test	**Requirement**	**Results**	**Samples Tested**
Drug Identity	Assay was conducted to verify the identity of beclomethasone dipropionate on the Model 3830 lead met known standard for BDP.	Passed *	3 lots of 29 leads
Drug Content/ Impurities	Assay was performed to identify and quantitate the drug impurities on the Model 3830 lead and to ensure that the product met internal specifications for finished goods release.	Passed *	3 lots of 29 leads
Drug Content Uniformity	Testing was conducted to verify process used reproducibility deposited drug material within a drug application lot. The lots were examined to ensure that they met the internal specification for drug content at the time of testing.	Passed *	3 lots of 29 leads
Stability	Leads were subjected to multiple thermal fluctuations (-45°C-70°C) and accelerated storage conditions (ASTM F1980-99 *Standard Guide for Accelerated Aging of Sterile Medical Device Packages*). After environmental stressing and accelerated aging, the specimens were evaluated for compliance to the drug content specification.	Passed *	29 leads in final package configuration
Residual Solvents	The amount of solvent used to apply the drug to the Model 3830 was evaluated to ensure that it was below the residual amount allowed by ICH Guidance Q3C	N/A	N/A
***In Vitro* Elution**	An assay was developed to measure the *in vitro* release kinetics of beclomethasone dipropionate from the Model 3830 lead. Specifications were based on the elution characteristics of leads evaluated in the clinical investigation. The product was evaluated to ensure that it met internal specifications	Passed *	4 lots of 30 distal tip subassemblies with steroid

	for finished goods release		
Sterilization	A 100% EtO sterilization process was used. It was considered an overkill sterilization cycle and was performed in accordance with accepted standards. Devices must have a sterility assurance level of at least 10^{-6}. Sterilization validation was performed by comparison to "worst case" devices.	Passed *	20 partial leads (Model 4068). Proximal and distal ends of leads were cut and capped to create a worst case condition.
* FDA's Center for Drug Evaluation and Research (CDER) determined that some tests were not conducted in accordance with widely accepted regulatory requirements and practice. As a condition of approval, the sponsor has agreed to work with FDA to further develop these processes.			

D. Canine Testing

The safety and biocompatibility of the Model 3830 lead was evaluated in a series of canine studies (**Table 6**). These studies were conducted in accordance with §21CFR 58 (Good Laboratory Practices). The results of these tests support the safety and biocompatibility of the Model 3830 Lead.

Table 6: Summary of Canine Studies

Study Number	Type/ Number of Animals	Number of Leads	Follow-up Duration/Procedure	Acceptance Criteria	Results
AR0120A0254	Canine Test / Control: 15 1 right atrial and 1 right ventricular lead	Test: 10 Control One: 10608 (no steroid) Control Two: 10609 (DXA)	Gathered electrical data at 0,1,2,3,4,8,12 weeks post implant 12 week histology	Acceptable electrical performance per design specification and in comparison to 5076 lead Acceptable histologic evaluation of electrodes	Acceptable comparison of Model 3830 to controls
AR0120A2254	Canine Test / Control: 9 2 right atrial leads and 2 right ventricular leads	Test: 32 Control: 16	7 days Blood and urine samples collected at least daily, Measured amount of beclomethasone dipropionate remaining on helix electrodes after repeated acute insertions and removals.	None. This study was performed to gain more insight into the pharmacokinetic and pharmacodynamic profile of BDP applied to the helix electrode of lead Model 3830.	The study did not show any detectable systemic blood levels of BDP. No steroid-related side-effects were observed.
S1028	Canine Test: 9 Control 4	No Leads were tested. Beclomethasone dipropionate was injected intravenously in	Blood Samples were collected at time 0, 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 8, 24, 48 and 72 hours Urine samples were collected at least daily	None This study was performed to evaluate the pharmacodynamic, pharmacokinetic, and any potential gross or histopathological	BDP is metabolized rapidly after a single IV dose. Biochemical and hematologic parameters were not

		doses of 1, 10, 100 and 1000ug per animal	3 day histology 7 day histology after 1000ug dose	effects of 4 dosages (1, 10, 100, and 1000 µg) of beclomethasone dipropionate (BDP) administered intravenously in canines.	remarkably changed after intravenous administration of BDP at four dosages in the dog. Pharmacodynamic monitoring failed to reveal adverse primary or secondary systemic effects of clinical relevance. There was no gross or histological evidence of splenic lymphoid tissue suppression, adrenal cortical atrophy or pituitary abnormalities within the animals examined.

X. Overview of Clinical Studies

The objective of the Model 3830 Lead clinical investigation was to demonstrate that the Model 3830 lead is safe and effective for atrial and ventricular pacing applications.

Study Design

This prospective, non-randomized, multicenter trial assessing the safety and effectiveness of the Medtronic Model 3830 Lead for the treatment of bradycardia pacing indications was conducted at 26 investigative centers in the United States (U.S.), four investigative centers in Canada and one center in Australia. Data from the Medtronic Model 5076 steroid-eluting lead clinical study was used as a historical control.

Patient Selection

Patient Inclusion Criteria:

- Candidates for implant must have standard indications for a dual chamber pacemaker

Patient Exclusion Criteria:

- Patients for whom a single corticosteroid dose may by contraindicated
- Patients with a mechanical tricuspid heart valve or history of tricuspid valvular disease
- Patients that are contraindicated for intravenous catheterization

- Patients who will not be geographically stable for the duration of the study follow-up period
- Patients unwilling to comply with the follow-up schedule
- Patients unwilling to sign an informed consent form

Patient Enrollment and Follow-Up

Data was collected for a total of 271 patients enrolled in the study. Of these patients, 264 underwent lead implant (86 roll-in and 178 non-roll-in). Follow-up was performed at pre-discharge (within 48 hours post-implant), two weeks, one month, and three months to meet study objectives. Patients will be followed at six months and every six months thereafter until the study closes. See

Figure 2 and

Figure 3 for enrollment and follow-up of the Model 3830 lead and the Model 5076 steroid-eluting lead (historical control).

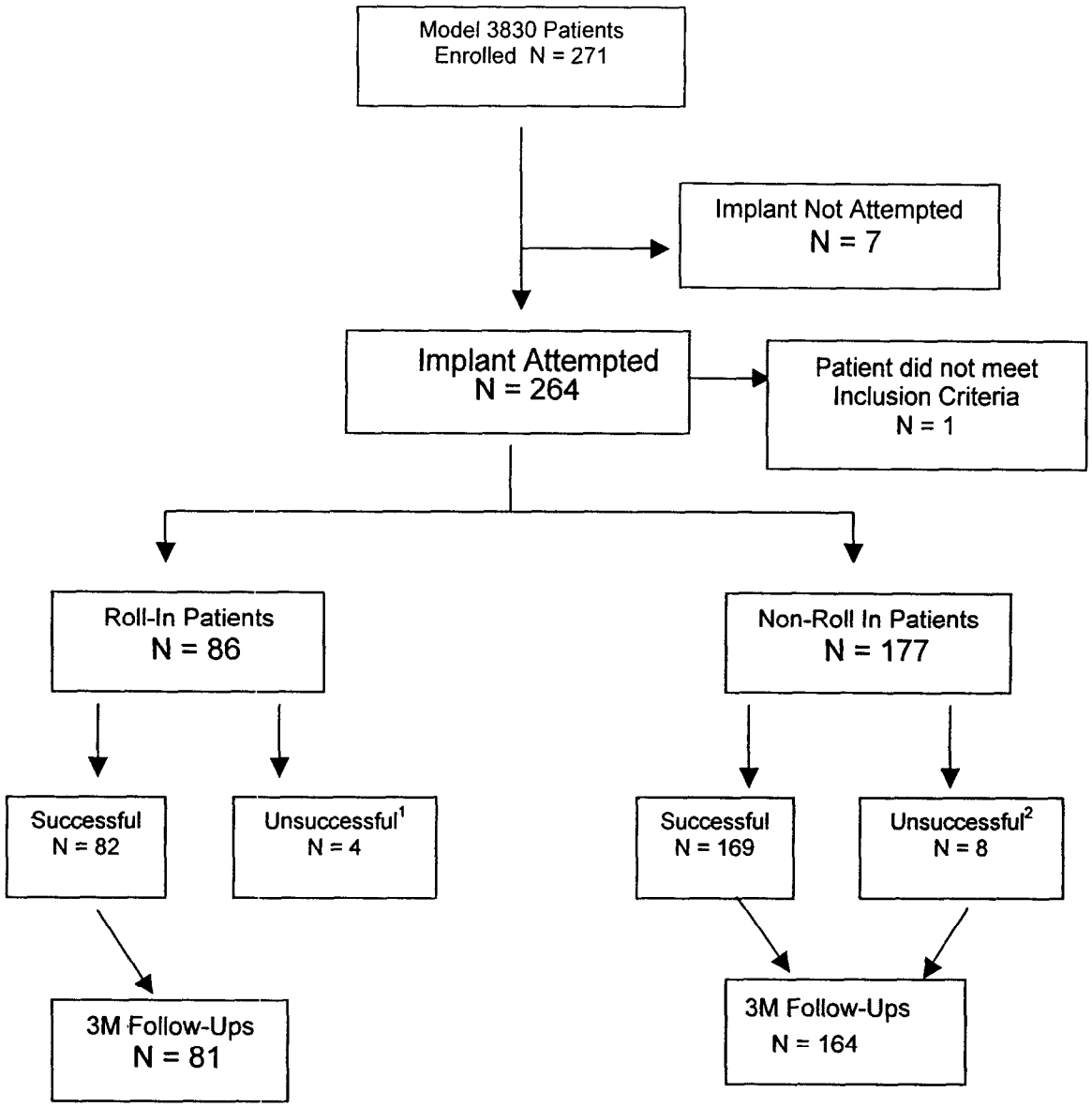

Figure 2: Enrollment and Follow-Up – Model 3830 Study Population

[1] Four patients with unsuccessful implants in the roll-in group did not receive a Model 3830 lead in either chamber and did not continue to be followed past implant.

[2] Five of eight patients had at least one Model 3830 lead implanted and continued to be followed per the protocol.

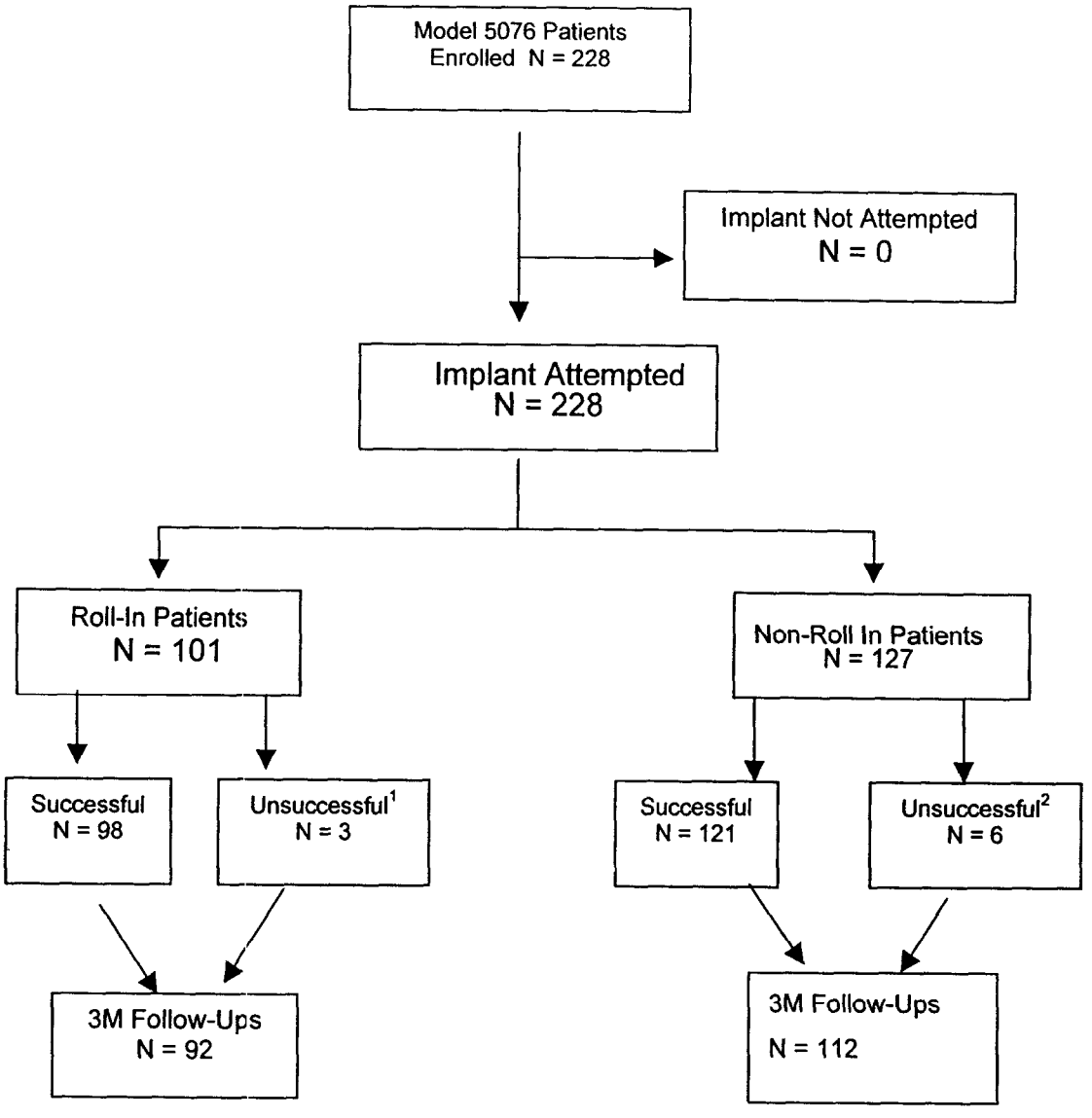

Figure 3: Enrollment and Follow-Up – Model 5076 Steroid-eluting Historical Control

[1] Three of three patients with unsuccessful implants in the roll-in group had at least one Model 5076 lead implanted and continued to be followed per the protocol.

[2] Five of six patients had at least one Model 5076 lead implanted and continued to be followed per the protocol.

Objectives

Primary Objective 1: Safety - Lead Related Complications

Hypothesis: The Model 3830 lead will have a clinically equivalent or superior survival from lead-related complications as compared to the Model 5076 steroid-eluting lead. Clinical equivalence is defined as a difference of 6% or less. This comparison will be made at three months post-implant. Atrial and ventricular lead related complications will be evaluated separately.

Primary Objective 2: Safety – Lead Related Events

Hypothesis: The Model 3830 lead will have clinically equivalent or superior survival from lead-related events as compared to the Model 5076 steroid-eluting lead. Clinical equivalence is defined as a difference of 10% or less. This comparison will be made at three months post-implant. Atrial and ventricular lead related events will be evaluated separately.

Primary Objective 3: Effectiveness - Pacing Performance

Hypothesis: The Model 3830 leads' atrial and ventricular pacing thresholds (pulse width threshold at 2.5V), will be clinically equivalent or superior to (less than) the Model 5076 steroid-eluting leads through three months post-implant. Clinical equivalence is defined as a difference of 0.06 ms or less. Atrial and ventricular thresholds will be evaluated separately.

Primary Objective 4: Effectiveness - Sensing Performance

Hypothesis: The Model 3830 leads' atrial and ventricular sensing amplitude measurements (P-and R wave amplitudes) will be clinically equivalent or superior to (greater than) Model 5076 steroid-eluting leads through three months post-implant. Clinical equivalence is defined as a difference of 1.5 mV or less for P waves and a difference of 3.0 mV or less for R-waves. Atrial and ventricular thresholds will be evaluated separately.

Secondary Objective 1: Pacing Impedance

The Model 3830 leads' atrial and ventricular pacing impedance will be collected and summarized from data collected through three months post-implant.

Secondary Objective 2: Lead and Catheter Handling

Physician response to lead and catheter handling characteristics questions will be collected and summarized.

Secondary Objective 3: Adverse Events in Roll-in Patients

The adverse events experienced in the roll-in Model 3830 patients were summarized. See section VIII, adverse events, for the summary information.

Demographic Data

Demographic data from non-roll-in Model 3830 patients appears in **Table 7**. Since roll-in patients are not included in the primary objective analyses, the summaries of data in this section pertain only to the non-roll-in patient population.

Table 7: Demographic Data (non-roll-in)

Gender (n, %)	
Male	101 (57.1%)
Female	76 (42.9%)
Age (years)	
Mean	70.8
SD	11.5
N	177
Indications	
Ventricular Rhythm Normal	132 (75%)
Non-Sustained VT	13 (7%)
Vent. Other Rhythm	39 (22%)
1st Degree Block	29 (16%)
2nd Degree Block	35 (20%)
3rd Degree Block	34 (19%)
Atrial Normal Rhythm	16 (9%)
Atrial Tachyarrhythmia	76 (43%)
Atrial Sinus Brady	111 (63%)
Cardiovascular History N(%)	
Exit Block	0 (0%)
CHF	27 (15%)
Previous MI	38 (21%)
Previous Cardiac Surgery	27 (15%)
Pacemaker Dependent	9 (5%)

Gender Bias

The gender selection in this clinical trial was completely random, and solely based upon exclusion and inclusion criteria. Men represented 57.1% of the population. The ratio of men versus women in this trial is reflective of the underlying distribution of the disease for the given age groups, ethnic groups and stages of disease in this population. No selection bias on the basis of gender was identified during the review. In addition, no differences in safety or effectiveness were found with respect to gender.

Data Analysis and Results

Table 8 provides the results of the primary and secondary objectives.

Table 8: Data Analysis and Results

Primary Objective	Results	Objective Met
1. Lead Related Complications		
A. Atrial	Number of leads 176 Number of pts with complications @ 3 months 3 Rate of Survival 98.29% Observed difference in survival (5076-3830) 0.09% 95% Upper Bound of Difference 2.62% Upper Bound Criteria ≤ 6%	Yes
B. Ventricular	Number of leads 177 Number of pts with complications @ 3 months 10 Rate of Survival 94.34% Observed difference in survival (5076-3830) 3.18% 95% Upper Bound of Difference 7.10% Upper Bound Criteria ≤ 6%	No
2. Lead Related Events		
A. Atrial	Number of leads 176 Number of pts with events @ 3 months 9 Rate of Survival 94.87% Observed difference in survival (5076-3830) 2.72% 95% Upper Bound of Difference 6.48% Upper Bound Criteria ≤ 10%	Yes
B. Ventricle	Number of leads 177 Number of pts with events @ 3 months 20 Rate of Survival 88.66% Observed difference in survival (5076-3830) 2.38% 95% Upper Bound of Difference 8.99% Upper Bound Criteria ≤ 10%	Yes
3. Pacing Performance		

Primary Objective	Results		Objective Met
A. Atrial Pulse Width Thresholds	N	170	Yes
	Least Squares Mean (ms)	0.070	
	Std. Error	0 009	
	Observed difference in survival (5076-3830)	0.002 ms	
	95% Upper Bound of Difference	0.026 ms	
	Upper Bound Criteria	≤ 0.06 ms	
B. Ventricular Pulse Width Thresholds	N	173	Yes
	Least Squares Mean (ms)	0.113	
	Std. Error	0.020	
	Observed difference in survival (5076-3830)	-0.030 ms	
	95% Upper Bound of Difference	0.015 ms	
	Upper Bound Criteria	≤ 0.06 ms	
4. Sensing Performance			
A. P-wave Amplitudes	N	170	Yes
	Least Squares Mean (mV)	2.88	
	Std. Error	0.25	
	Observed difference in survival (5076-3830)	0.48 mV	
	95% Upper Bound of Difference	1.204 mV	
	Upper Bound Criteria	≤ 1.5 mV	
B. R-wave Amplitudes	N	173	Yes
	Least Squares Mean (mV)	11.36	
	Std. Error	0.97	
	Observed difference in survival (5076-3830)	-0.65 mV	
	95% Upper Bound of Difference	1.578 mV	
	Upper Bound Criteria	≤ 3.0 mV	

The overall ventricular lead related complication rate exceeded the Model 5076 steroid-eluting lead. Four ventricular lead related complications occurred in the first 37 non-roll-in system implants (10.8% rate). After interim review of the data and modification to the implant technique recommendations, an additional 140 patients were enrolled in the non-roll-in population, of which 6 additional ventricular lead related complications occurred (4.3% rate).

Device Failures and Replacements

A total of 16 leads were removed from all study subjects (including roll-in patients) before the data cutoff date. Four removals were due to lead dislodgement, one was due to high thresholds, two due to pericardial effusion, two due to nonspecific complaints of pain, two leads were removed from one patient due to possible infection, two leads were removed during an upgrade to a bi-ventricular pacing system, one lead was removed due to transversing a patient foramen ovale into the left atrium and two were removed prophylactically along with the other lead's removal. None of the

devices returned to Medtronic for analysis showed any defects that would have caused device failure.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

Safety of the Medtronic® SelectSecure™ Lead Model 3830 was characterized by evaluating the lead in bench and animal studies, and by examining survival from lead-related complications and events in a clinical trial. Survival from all complications and events at 3 months post-implant was determined to be acceptable in this study. Although the primary objective for ventricular lead-related complications was not met, modified implant techniques were implemented with a corresponding decrease in ventricular complications that was in alignment with current Medtronic marketed leads.

Effectiveness of the Medtronic® SelectSecure™ Lead Model 3830 was characterized by evaluating the lead in bench and animal studies, and by examining pacing and sensing performance through three months post-implant in a clinical trial. The 3830 lead demonstrated that it was statistically equivalent to the Model 5076 steroid-eluting lead with respect to atrial and ventricular pulse width thresholds, P-wave amplitude, and R-wave amplitude.

Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Panel, and FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

CDRH approved this PMA application on August 3, 2005.

The effectiveness of the lead was shown in the results of the clinical trial; the Model 3830 leads' atrial and ventricular sensing amplitude measurements (P-and R wave amplitudes) were clinically equivalent to Model 5076 steroid-eluting leads through three months post-implant.

Therefore, while there were still some manufacturing and test method concerns remaining, CDRH decided that these concerns do not affect the safety of the device, and the remaining concerns could be conveyed to the sponsor post-approval. To improve their manufacturing specifications, the sponsor agreed to

work with FDA to address issues related to finished product specifications, test methods, product release testing, in vivo-in vitro correlations, and the certificate of analysis for the 3830 lead.

CDRH believes that the sponsor has adequately addressed all of FDA's questions related to the safety and effectiveness of the lead.

The applicant's manufacturing facilities were inspected and were found to be in compliance with the Quality System Regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.